ORIGINAL ARTICLE

Association of Sleep Disordered Breathing with Systemic hypertension – The Indian perspective

Kavita R. Mody, Amita U. Athavale, Maheema A. Bhaskar , R. Mohan, Kapil Salgia

Department of Chest Medicine and EPRC, Seth G.S. Medical College and KEM Hospital, Mumbai-400012

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Abstract

Introduction : Economic growth, better per capita income and a westernized lifestyle has increased the prevalence of metabolic disorders like hypertension, diabetes, dyslipidemia and obesity in developing countries including India. Sleep Disordered Breathing has been found to be increasingly associated with obesity and hypertension. The incidence and prevalence of SDB in India remains to be fully investigated. In the study an attempt was made to elucidate the true extent and magnitude of association between sleep disordered breathing and hypertension in Indian context.

Materials and Methods : 80 patients were enrolled from the Chest Clinic of a tertiary hospital from 2003 till 2005. Patients underwent clinical interview (questionnaire), physical examination, blood pressure measurement and routine investigations. Overnight sleep study was carried out using E series EEG/PSG Compumedics machine (Compumedics, Australia) at the sleep lab.

Results : Mean systolic and diastolic blood pressure as well as prevalence of hypertension increased significantly with increasing SDB. High body mass index may be a confounding factor in the analysis. OSAHS has been identified as an independent risk factor for hypertension, with a linear relationship between hypertension and OSAHS. AHI was strongly associated with self reported history of snoring (p=0.007).

Conclusion : Our findings suggest that sleep disordered breathing is associated with systemic hypertension in middle and older individuals.

Keywords : hypertension, sleep disordered breathing, sleep study

Introduction

Sleep Disordered Breathing (SDB) has generated major interest recent times. Studies from large American and European multicentric cohorts have suggested that roughly 1 in every 5 adults have mild obstructive sleep apnea (OSA) and 1 in 15 have moderate OSA. The prevalence was higher in white men and women with BMI of 25 to 28[1]. Findings from early cross sectional studies with OSA, hypertension, myocardial infarction, and other cardiovascular diseases were mixed and generated considerable criticism. Few studies have established a causal relationship between SDB and systemic hypertension. Large scale studies into the epidemiology of sleep disordered breathing in India are few. Hypertension is a silent killer with increasing prevalence in India due to lifestyle changes and urbanization. This study aims to determine the true extent and magnitude of association between sleep disordered

Address for Correspondence:
Kavita Mody
M.D. ex-registrar
Department of Chest Medicine and EPRC
Seth G.S. Medical college and KEM Hospital,
Mumbai - 400012.
E-mail: kavitamody@gmail.com

breathing and hypertension in Indian context. This small cohort analysis generates adequate evidence so that larger population based studies may be planned.

Material and methods

An observational study of adult patients referred for sleep disordered breathing from 2003 till July 2005 was carried out in the Chest clinic of a tertiary care hospital in Mumbai, India. 80 adult patients of either sex were recruited for the study after an informed consent. The presenting symptoms ranged from snoring, witnessed apneas, excessive daytime somnolence, headache, sleep related arousals, and falling asleep while driving. Unstable patients, patients with decompensated cardiopulmonary disease, stroke, recent surgery of upper respiratory tract and pregnant mothers were excluded from the study.

The enrolled patients were critically reviewed with a pre designed questionnaire. An initial meticulous clinical history was taken with emphasis on associated medical illness like systemic hypertension, hypothyroidism, coronary artery disease and other respiratory diseases. Blood pressure was measured in the right upper arm in sitting position with the patient relaxed and the appropriate sized pressure cuff used. BP was monitored with a mercury manometer on two different occasions approximately 1 week apart after patients had rested quietly for 10 minutes. Hypertension was defined as systolic blood pressure of $\geq$ 140 mmHg and /or diastolic blood pressure $\geq$ 90 mmHg on two occasions in absence of any antihypertensives.

All the patients were referred to ENT surgeons for examination of the upper airway for any abnormality that could contribute to airway narrowing such as a nasal polyp or a small oropharyngeal airway. An endocrine and cardiac evaluation was done in relevant cases.

Body mass index (BMI) was then calculated for each patient as follows:

$$BMI = Weight\ (kg) / Height^2\ (m)$$

Obesity was graded as per the World Health Organization[2] Asian Perspective categories.

BMI	
18.5 – 22.9	Normal
23.0 – 24.9	at Risk
25.0 – 29.9	Grade 1 obesity
> 30.0	Grade 2 obesity
> 40.0	Grade 3 obesity

The neck circumference was measured at the level of the cricohyoid membrane.

No acclimatisation study was done. All patients underwent a polysomnography using 24 channels PSG/ EEG E Series Compumedic machine (Compumedics, Australia). A minimum of seven hours recording per patient was done. The parameters monitored simultaneously were the electrocardiogram, electroencephalogram, electromyogram, electro-oculogram, finger pulse oximetry, chest and abdominal excursions using respiratory inductance plethysmography, airflow by oronasal thermocouples, body position and leg movements.

Sleep disordered breathing was assessed using Apnea Hypopnea Index defined as the average number of apnea and hypopneic episodes per hour of sleep. Apnea was defined as cessation of airflow for minimum of 10 seconds associated with sleep fragmentation, EEG arousal and a 4% drop in saturation. Hypopnea is defined as the 50% reduction in airflow which is terminated by either an arousal or a 4 % decrease in saturation.

Statistical analysis

All the variables were analysed using SPSS software (Chicago, Illinois Inc.). The means and proportions were analysed using analysis of variance and chi square test respectively. The relation between the OSA variables and blood pressure were done by multiple linear regression.

Results and observations

Descriptive characteristics of the study population are described in Table 1. Compared with those of lower AHI values, participants with higher AHI levels included larger proportion of men in the middle age group (40-60 yrs). Alcohol consumption and smoking status did not appear to make significant correlation with AHI. Out of 80 patients 39 had sleep disordered breathing (AHI $\geq$5).

Body mass index showed significant correlation (95% CI, P = 0.004) with severity of sleep disordered breathing with severity increasing at higher BMI. Similarly neck circumference also showed positive correlation (95% CI, P=0.075) with severity of OSA. Increasing neck circumference showed patients had increasing SDB. Table 2 describes the BMI characteristics of patients with SDB.

Table 1: Distributions of the selected characteristics of the study population

	CHARACTERISTIC	Total	AHI CATEGORY				
			<5	5-15	15-30	≥30	Pvalue
1) Men(%)		72.6	37.5	11.3	13.8	10	**0.649**
2) Age	20-40 yrs,(%)	24.4	16.7	1.3	1.3	5.1	**0.024**
	40-60 yrs,(%)	59.1	32.1	9.0	10.3	7.7	
	60-80 yrs,(%)	16.7	2.6	7.7	3.8	2.6	
3) Alcohol intake	Yes,(%)	33.8	16.3	10.0	5.0	2.5	**0.163**
	No,(%)	66.2	35.0	7.5	11.3	12.5	
4) Smoking	Yes,(%)	47.6	27.5	10.0	8.8	1.3	**0.033**
	No,(%)	52.4	23.8	7.5	7.5	13.0	

Table 2: BMI & Neck circumference characteristics in study population

	CHARACTERISTIC	Total	AHI CATEGORY				
			<5	5-15	15-30	>30	Pvalue
BMI, (%)	< 25	2.5	2.5	0	0	0	**0.004**
	25 -30	40.1	26.3	7.5	5	1.3	
	>30	57.8	22.6	10.1	11.3	13.8	
Neck circumference inch, (%)	10 -15	20.6	19.2	6.8	0	1.4	**0.075**
	15 -20	69.8	30.1	11	16.4	12.3	
	>20	2.8	1.4	0	0	1.4	

Higher AHI correlated significantly with symptoms such as sleep related arousals (95% CI, P = 0), EDS (95% CI, P = 0.178), nocturia (95% CI, P = 0.00), drooling of saliva (95% CI, P = 0.001) and headache (95% CI, P = 0.013). Table 3 describes the major symptom complexes with SBD.

Table 3: Symptoms and corelation with AHI

SYMPTOM		AHI CATEGORIES				
		<5	5-15	15 -30	>/=30	p value
SNORING, (%)	YES	35	16.3	16.3	15	**0.007**
	NO	16.3	1.3	0	0	
SLEEPRELATED AROUSALS, (%)	YES	16.3	11.3	16.3	11.3	**0.000**
	NO	35	3.8	0	3.8	
EDS, (%)	YES	27.5	11.3	13.8	11.3	**0.178**
	NO	23.8	6.3	2.5	3.8	
NOCTURIA, (%)	YES	10	8.8	12.5	8.8	**0.001**
	NO	41.3	8.8	3.8	6.3	
DROOLING, (%)	YES	2.5	5	8.8	6.3	**0.001**
	NO	48.8	12.5	7.5	8.8	
AFFECTED ACTIVITIES, (%)	YES	16.3	8.8	11.3	8.8	**0.071**
	NO	35.0	8.8	5.0	6.3	
HEADACHE, (%)	YES	10.0	5.0	10.0	60.3	**0.032**
	NO	41.3	12.5	6.3	8.8	

AHI strongly associated with self reported history of snoring (95% CI, P = 0.007).

There is significant correlation of diagnosed hypertensives with AHI. Patients suffering from hypertension had higher AHI values. 10 patients (12.5%) had AHI values in the range of 5 - 15, 8 patients (10%) had values in the range of 15 - 30 and 11 patients (13.8%) had AHI > 30. Analysis showed a significant direct correlating of actual blood pressure values with AHI (Table 4, 5).

Table 4: Correlation of blood pressure with AHI

AHI / HTN, (%)	<5	5 -15	15 -30	>30
YES	20.0	12.5	10.0	13.8
NO	31.3	5.0	6.3	1.3

Chi square test significant p = 0.006

Table 5: Correlation of severity of hypertension with AHI

BP sys/dias, (%)	AHI			
	<5	5 -15	15 -30	>30
<120/<80	30	3.8	8.8	3.8
120-140/80-90	12.5	6.3	1.3	5.0
140-160/90-100	8.8	7.5	6.3	5.0
>160/>100	0	0	0	1.3

Chi square test significant p = 0.061

24 (30%) patients with BP ≤120/80 had no SDB. In patients with BP of 140/90, 16 (20.1%) had SDB while 7 (8.8%) did not have SDB. AHI was linearly associated with blood pressure values. However multiple regression analysis showed that these associations were partially explained by BMI (Table 6). Age showed significant correlation other than BMI. However since the study population is a small, the results are to be interpreted with caution.

Discussion and conclusion

It has been estimated that about 20-50% of patients with arterial hypertension have obstructive sleep apnea[3-5]. Similarly, the prevalence of hypertensive patients with sleep disordered breathing has been found to be between 40-80%[6-8]. Inspite of the casual association between sleep disordered breathing and hypertension, doubts have been raised due to confounding factors such as age, sex, obesity etc. However epidemiological studies and intervention trials showing successful treatment of sleep apnea by means other than weight loss is accompanied

Table 6: Linear regression analysis of blood pressure on measures of Sleep disordered breathing

	Systolic B P		Diastolic B P	
	ß	P value	ß	P value
AGE	0.327	0.005	0.138	0.069
BMI	0.263	0.221	0.255	0.076
NC	-0.590	0.446	0.009	0.986
AHI	0.107	0.270	0.015	0.820

by a significant decrease in both daytime and nighttime blood pressure, support the hypothesis of independent causal association between sleep apnea and hypertension. In the Sleep Heart Health Study, a multicentric prospective study of SDB and risk for hypertension, the apnea hypopnea index in 6132 participants aged above 40 years was associated with the hypertension [odds ratio(OR),1.37; 95% CI, 1.03-1.83] comparing the highest and lowest categories, after adjusting for potential confounding factors[9]. In a prospective population based study of the association between objectively measured SDB and hypertension, the authors analysed data on SDB, blood pressure, habitus, and health history at baseline and after four years of follow-up in 709 participants of the Wisconsin Sleep Cohort Study[10]. The OR's for the presence of hypertension at the four- year follow- up study according to the AHI at the baseline were estimated after adjustment of baseline hypertension status, body- mass index, neck and waist circumference, age, sex, and weekly use of alcohol and cigarettes. Relative to the reference category of AHI of zero event per hour at baseline, the OR's for the presence of hypertension at the follow- up were 1.42 (95%CI, 1.13 to 1.78) with an AHI of 0.1 to 4.9 events per hour at baseline as compared with none, 2.03 (95%CI, 1.29 to 3.17) with on AHI 5 to 14.9 events per hour, and 2.89 (95%CI, 1.46 to 5.64) with an AHI of 15.0 or more event per hour. This dose-response association between SDB at baseline and the presence of hypertension four years later was independent of known confounding factors suggesting that SDB is likely to be a risk factor for hypertension and consequent cardiovascular morbidity in the general population.

Out of 80 patients included in the study, 58 were male and 22 were females. Of 58 males, 28 had SDB while 11 females had SDB. Patients ranged from 20 to 80 years with higher incidence of SDB in patients in their 5th to 7th decades of life which corroborates with the study of Ancoli Israel et al[11] and Bixler et al which states that the prevalence is two to three times higher in older age group compared to middle age[12].

Self reported snoring has been shown to have strong association with sleep apnea in most reports. Snoring was present in 66(82.5%), out of which 38 (57.5%) had SDB. In study conducted by Deegan and Mc Nicholas the predictive value of positive or negative history were 63% and 56% respectively[13]. Also Stradling and workers have reported a 5-fold increase in daytime sleepiness with increased snoring[14]. Snoring related arousals, choking, gasping and observed apneas were seen in 55% patients of whom 70.54% were diagnosed to have SDB. This correlates with finding of the study of Dixon & Linda[15]. Excessive daytime somnolence was present in 63.8%of which 56.86% were diagnosed to have SDB. Excessive daytime somnolence as a symptom is commonly associated with increasing severity .Excessive daytime somnolence has been found to be having a strong correlation with SDB which was corroborated in our study also. In our study 40%of patients had nocturia. It has been reported that one third of patients would have nocturia.

In our study out of the 80 patients 2.5% had BMI <25,40% had between 25 to 30, 33.8% between 30 to 35 ,12.5% between 35 to 40 and 11.3% had BMI more than 40.Young et al found that an increase in BMI more than 1 standard deviation increases the chance of SDB by four fold[16]. Guilleminault et al in their study found that three fourth of the patients with SDB were obese[17]. In our study also, we found that as BMI increases the severity of SDB also increases in the form of AHI. Straddling et al in their study found a clear relationship between excess body weight usually expressed as BMI and number of sleep related respiratory disturbances corroborates with our study[18]. P value of 0.004 indicates that BMI correlates statistically significantly with AHI. Excess visceral fat is a characteristic feature of metabolic syndrome X i.e. a constellation of abnormalities including insulin resistance, dyslipidemia, inflammation, hypertension and so forth. Clustering of these metabolic factors increases the risk of many cardiovascular diseases. Central adiposity and visceral fat deposition appear to be the hallmark of increased risk of OSA. The stigmata of syndrome X should therefore be broadened to incorporate OSA – the new Syndrome Z[19].

Neck circumference has been found to be a good predictor of OSAHS. Though in our study p value was not significant however higher neck circumference values did show higher SDB levels.

OSAHS has been identified as an independent risk factor for hypertension, with a linear relationship existing between hypertension and OSAHS. An increase in severity of OSAHS by 1 AHI /hour increases the odds of hypertension by 1%.

Although limited by small sample size, this study has demonstrated an association between OSA and hypertension. It has been shown that treated or untreated hypertensives are more likely to have AHI >5 than normotensives. The results of this study have indicated that the relationship between hypertension and OSA is partly due to confounding by the common risk factors. Worsnop CJ, Naughton MT et al concluded similar results in their study[20]. Grunstein and coworkers also found that in subjects with OSA, AHI was a determinant of blood pressure independent of obesity. Carlson and coworkers found that OSA, age and obesity were independent risk factors for hypertension[21]. An increased prevalence of OSA and hypertensives compared with that in normotensives matched for age and percentage of ideal body weight has been found. As expected, controlling for BMI diminished the strength of association between estimates of sleep disordered breathing and hypertension.

Our results support the common concept of obesity as a possible confounder of the putative association between sleep disordered breathing and hypertension. The true level of association between the sleep disordered breathing and hypertension may lie between the unadjusted estimates and BMI – adjusted estimates. Nonetheless given the observational nature of the study, the possibility due to unmeasured or unknown confounders cannot be ruled out. Young et al in a large cross sectional study have clearly associated sleep disordered breathing with systemic hypertension in middle aged and older individuals of different sexes and ethnic backgrounds[22].

In the population-based study conducted by Khin Mae Hla, Terry B. Young et al found that the log odds of hypertension varied linearly with apnea hypopnea index across the range of mild to moderate sleep apnea in the model[23]. Odds ratios ranged from 2.0 to 5.0 for hypertension associated with an apnea hypopnea index of 5 to 25 compared with that of an apnea hypopnea index of less than 5 in a dose response fashion.

The mechanism underlying the association between sleep disordered breathing and hypertension are not entirely clear. Several have been proposed including hemodynamic disturbances resulting from intermittent negative intrathoracic pressure during apneic episodes, recurrent episodes of hypoxemia and hypercapnea resulting in abnormal activation of arterial chemoreceptors and increased sympathetic activity associated with repeated arousals during sleep.

In summary, this study suggests an association between sleep disordered breathing and hypertension among middle aged participants. However in view of small population group, results should be interpreted with a caution.

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